

# Histopathological Study of Whipple's Resected Specimens at a Tertiary Care Centre.

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## ABSTRACT

**Background:** Pancreatic cancer is one of the most important causes of death in eastern countries and the fourth cause of death from cancer in the western hemisphere. Whipples is the most acceptable operation for performing in various malignant and benign diseases of pancreas and periampullary area. **Aim:** To study the Histopathological spectrum of lesions in Whipple's specimens received over a period of two years in our institution. **Methods:** This is a retrospective study of 24 whipple's resected specimens received of both malignant and non malignant lesions between June 2016 – June 2018. After receiving specimens, gross examination was noted in records, and specimens were processed for Histopathological examination. After confirmation of diagnosis by HPE, those findings were noted in records. After routine processing all the tumours are reported according to CAP protocol (2011). Out of 24 specimens diagnosed by HPE, 10 (41.6%) were diagnosed as Ampullary and periampullary carcinoma (Adenocarcinoma), 7 (29.1%) were chronic pancreatitis, 2 (8.3%) each of specimens were diagnosed as pancreatic ductal adenocarcinoma, neuroendocrine carcinoma, acinic cell carcinoma, and 1 (4.1%) was pseudopapillary tumor of pancreas. Out of 10 Adenocarcinoma specimens, 8 (80%) cases were reported as well differentiated adenocarcinoma and 2 (20%) cases were reported as moderately differentiated adenocarcinoma. **Conclusion:** Adenocarcinoma was predominant histological type encountered in elderly population with equal sex ratio. All carcinoma specimens were predominantly observed among > 40 years patients. Well differentiated is the common histologic subtype. Grossing is very crucial in the analysis of whipples resected specimen's.

**Keywords:** Ampullary and PeriampuWhipples procedure.

## INTRODUCTION

Whipple's procedure or Kausch-Whipple procedure involves removal of wide part of head of pancreas, duodenum from the pylorus to the ligament of Teitz, proximal jejunum, distal extrahepatic biliary tract, Gallbladder along with cystic duct and occasionally Distal part of stomach.<sup>[1]</sup>

In 1935, Allen Oldfather Whipple modified the procedure of Pancreaticoduodenectomy by doing one stage procedure involving removal of complete excision of head of pancreas and whole of duodenum.<sup>[2]</sup> Whipples is the most acceptable operation for performing in various malignant and benign diseases of pancreas and periampullary area.<sup>[3]</sup>

Pancreatic cancer is one of the most important

causes of death in eastern countries and the fourth cause of death from cancer in the western hemisphere. Only a few percent of patients can survive from this condition for more than 5 years. Most patients present with an advance stage of the disease, and only in 10% to 20% of them the mass is resectable.<sup>[4]</sup>

About 5% of the gastrointestinal malignancies are constituted by ampullary and periampullary carcinomas. Most part of the tumour located in the ampullary region which bulges in to duodenal mucosa considered as Ampullary carcinoma. If the tumour is involving circumference of ampulla then it is considered as periampullary carcinoma.

Pancreaticoduodenectomy, also known as whipple's procedure is done for Periampuillary and ampullary carcinoma, Tumours of head of the pancreas and pancreatic duct, Tumours of common bile duct, Duodenal malignancies. Sometimes this surgery may perform in non malignant conditions such as chronic fibrosing pancreatitis, paraduodenal pancreatitis and chronic pancreatitis.

Prognosis of Pancreatic cancers can be predicted by some factors such as size of the tumour, degree of

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differentiation, status of resected lymph nodes, and the involvement of the resected margins, the post-resection CA 19-9 level and tumor DNA content. Among various treatments for pancreatic cancers, surgery was the only chance for cure.<sup>[5]</sup>

Predisposing factors for pancreatic cancer is remaining unknown, but risk increases with longer exposure to smoke and greater tobacco usage. There is some evidence that alcohol, coffee, and aspirin consumption are among the predisposing factors. Other risk factors are history of diabetes or chronic pancreatitis, chronic cirrhosis, and patients with blood type A, B, or AB. Only 5% to 10% of these patients have a positive familial history of pancreatic cancer.<sup>[6]</sup>

To study the Histopathological spectrum of lesions in Whipple's specimens received over a period of two years in our institution.

## MATERIALS AND METHODS

This is a retrospective study of 24 Whipple's resected specimens received of both malignant and non malignant lesions between June 2016 – June 2018, conducted at Department of Pathology, Government Medical College, Kurnool. All the data related to age, sex, surgical procedure, gross examination, HPE report were gathered from old medical records. After receiving specimens, gross examination was noted in records, and specimens were processed for Histopathological examination. After confirmation of diagnosis by HPE, those findings were noted in records. After routine processing all the tumours are reported according to CAP protocol (2011).

Grossing Protocol: When most part of the tumor is located in the ampullary region and bulges into the duodenal mucosa stretching it, it is taken as ampullary carcinoma. A tumor that involved the circumference of the ampulla was taken as periampullary carcinoma. A tumor that involved the circumference of the common bile duct [CBD] was taken as common bile tumors. A tumor with the base or the epicenter in the duodenum and not involving the ampulla was taken as duodenal carcinoma.

Specimen is opened along the greater curvature of stomach, anterior wall of pylorus, greater curvature of duodenum. The probe should be placed in the common bile duct towards the ampulla. Similarly the probe should be placed along the main pancreatic duct. The ducts were opened along longitudinal paths of probe. Assess the tumour arising from biliary, intrapancreatic to ductal system. Tumor size, consistency, macroscopic appearance of each organ of a specimen & its measurements, cystic neoplasms of duct, spongy areas and necrotic findings were noted.

Intestinal type arises from intestinal mucosa of papilla. Those arise from ductal epithelium penetrates duodenal muscularis propria. Grading of tumors were given as: >95% - well, 50 - 95% -

moderately, 5-49% - poorly, Less than 5% - undifferentiated.

Histopathological Examination: During HPE slides examination, diagnosis, grading, tumor budding, staging, nodal status, perineural invasion, angioinvasion and marginal status were assessed. The grading of adenocarcinoma was done based the percentage of glands seen in the tumor tissue. If there were >95% glands it was taken as well differentiated, 50- 95% glands as moderately differentiated grade, 5-49% as poorly differentiated grade and <5% as undifferentiated adenocarcinoma.

The staging of the Ampullary carcinoma was based on AJCC TNM classification. T1 - If the tumor is limited to the ampulla or sphincter of Oddi. T2- If the tumor invades the duodenal wall. T3- If the tumor invades the pancreas and T4- If the tumor invades the peripancreatic soft tissue or adjacent structures. N1- If there is regional nodal metastasis. In the case of Endocrine neoplasm, the following staging was followed. T1- If the tumor is limited to the pancreas and it is less than 2cm in diameter. T2 - If the tumor is restricted to the pancreas and size is between 2-4 cm. T3 - If the tumor is more than 4 cm diameter if it is limited to the pancreas or if the tumor invades the duodenum or the bile duct. T4- If the tumor invades the adjacent organs. N1- If the regional nodes are involved by the tumor. In case of the solid pseudo papillary tumor T1- When the tumor is limited to the pancreas and was less than 2cm in diameter. T2- When the tumor is limited to the pancreas and more than 2cm in diameter. T3- When the tumor invades duodenal, peripancreatic tissue and the bile duct. T4- When the tumor invades the other structures.



Figure 1: Showing Gross Examination protocols

## RESULTS

A total of 24 Whipple's resected specimens were processed and analysed. Out of 24 specimens



diagnosed by histopathological examination, 10 (41.6%) were diagnosed as Ampullary and periampullary carcinoma (Adenocarcinoma), 7 (29.1%) were chronic pancreatitis, 2 (8.3%) each of specimens were diagnosed as pancreatic ductal adenocarcinoma, neuroendocrine carcinoma, acinic cell carcinoma, and 1 (4.1%) was pseudopapillary tumor of pancreas.

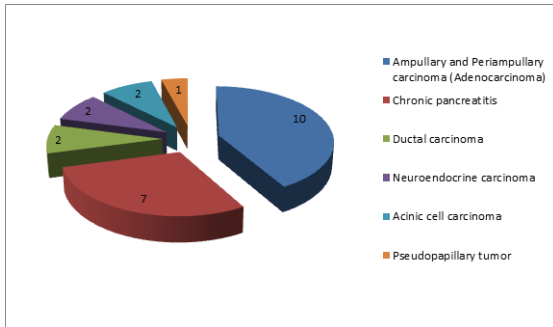


Chart 1: Distribution of HPE Diagnosis



Figure 2: Gross picture showing ampullary carcinoma



Figure 3: Gross picture showing Chronic necrotizing pancreatitis

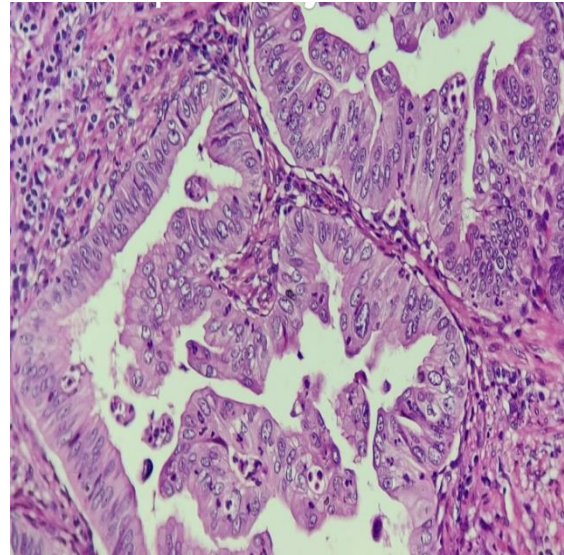


Figure 4: Peri Ampullary carcinoma

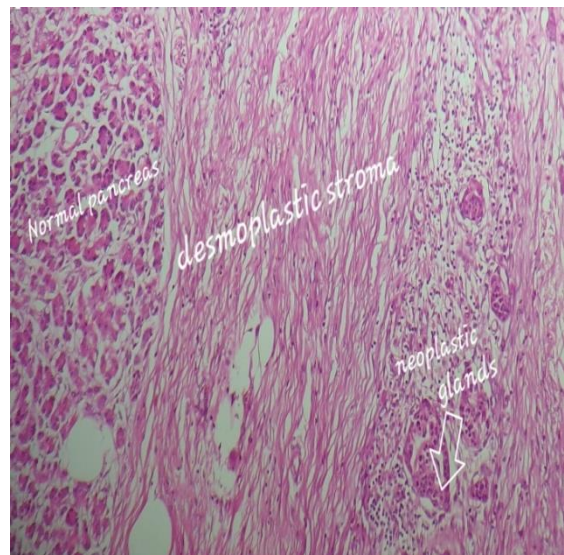


Figure 5: Pancreatic ductal adenocarcinoma

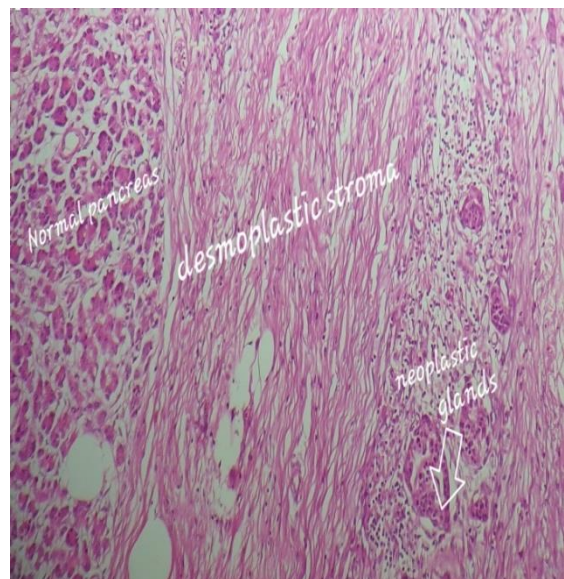


Figure 6: Neuroendocrine carcinoma



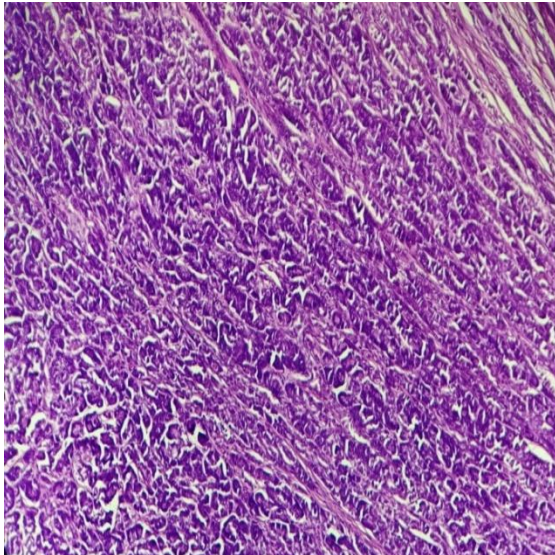


Figure 7: Acinic cell carcinoma

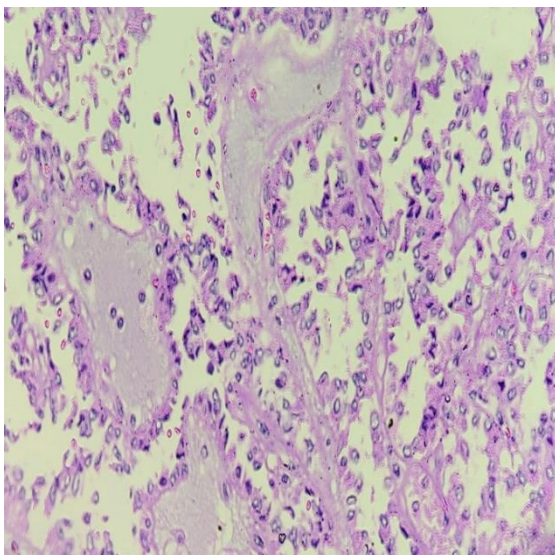


Figure 8: Solid Pseudopapillary tumor of Pancreas



Figure 9: Chronic Pancreatitis

All Ampullary and periampullary carcinoma specimens were diagnosed histopathologically as adenocarcinoma.

Adenocarcinoma was predominantly observed in patients aged >60 years. 5 (50%) out of 10 ampullary and periampullary carcinoma of pancreas diagnosed in the age group of >60 years, 3 (30%) in patients aged 31- 40 years and remaining 2 (20%) in patients aged 41- 50 years. 4 (57.1%) out of 7 chronic pancreatitis were observed in patients aged 51-60 years and remaining 3 (42.8%) were noted in 21-30 years of age. Acinic cell carcinoma, neuroendocrine carcinoma was observed in patients aged 41-50 years. Ductal carcinoma was observed in patients aged 51-60 years. Pseudopapillary tumor of pancreas is observed in 20 years old patient.

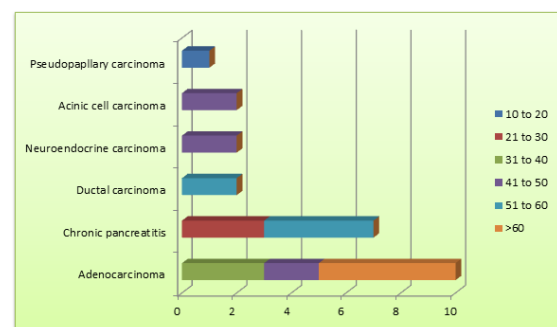


Chart 2: Age wise distribution of HPE diagnosed Whipple's resected specimens

Out of 10 Adenocarcinoma specimens, 8 (80%) cases were reported as well differentiated adenocarcinoma and 2 (20%) cases were reported as moderately differentiated adenocarcinoma. Lymphovascular and perinuclear invasion (10%) was seen in one case each

On assessment of staging of 10 ampullary and periampullary carcinoma cases, 7 are under T2, 2 are at T3 staging, 1 case was T1, and 1 case was categorised as N1.

## DISCUSSION

Pancreas is the organ situated in retroperitoneum, many patients come to the hospital in an advanced stage. Surgery is the cornerstone of treatment of these patients with biliary stenting and chemotherapy playing a supportive role. Whipple's procedure is also performed for non-malignant indications for relief of obstructive jaundice, pain or vomiting. On estimation of five year survival rate of patients who undergo Whipple's procedure was 10–25%.<sup>[7]</sup>

In United States, pancreatic malignancy is the fourth most common fatal malignancy,<sup>[8]</sup> and 6th most common fatal malignancy in Europe.<sup>[9]</sup>

Most probable predisposing factors of pancreatic malignancy are smoking and tobacco usage. The risk is directly proportional to the number of pack years.

Other less significant risk factors are chronic pancreatitis, diabetes, obesity and occupational exposure. Hereditary risk factors are Familial Pancreatitis, Peutz Jeghers syndrome, Familial atypical mole and multiple melanoma syndrome, cystic fibrosis.<sup>[10]</sup>

Out of 24 specimens diagnosed by histopathological examination, 10 (41.6%) were diagnosed as Ampullary and periampullary carcinoma, 7 (29.1%) were chronic pancreatitis, 2 (8.3%) each of specimens were diagnosed as pancreatic ductal adenocarcinoma, neuroendocrine carcinoma, acinic cell carcinoma, and 1 (4.1%) was pseudopapillary tumor of pancreas in the present study. In our study, all Ampullary and periampullary carcinoma specimens were diagnosed histopathologically as adenocarcinoma.

In similar to our study, Max Schimdt et al.<sup>[11]</sup> demonstrated pathological examination, noted 57% periampullary carcinoma, 22% chronic pancreatitis, 12% cystic neoplasms, 4% islet cell neoplasms and 5% others. Gupta BB et al.<sup>[12]</sup> reported 39.21% adenocarcinoma of pancreas, 27.45% adenocarcinoma of duodenum, 7.8% of solid pseudopapillary neoplasm of pancreas, 11.76% cholangiocarcinoma of terminal CBD, 7.8% of chronic pancreatitis, 5.88% of serous adenoma of pancreas. Shifa Seyed Ibrahim et al.<sup>[13]</sup> noted 21 (70%) out of 30 cases had ampullary and periampullary carcinoma, which was very high rate, followed by 6.6% pancreatic endocrine tumors, 20% chronic pancreatitis, 3.3% solid pseudopapillary tumour of pancreas. In western population, Landis S H et al.<sup>[14]</sup> noted pancreatic adenocarcinoma was most common among the Whipple's specimen. Manan Shah et al.<sup>[15]</sup> reported among malignant lesions, 71 (68.93%) were peri-ampullary, 15 (14.56%) were pancreatic, 11 (10.67%) were duodenal and only 6 (5.825%) were cholangiocarcinoma. Malignant (93.63%) lesions outweighed benign lesions (6.36%) and also observed adenocarcinoma histology subtype predominantly in ampullary tumors.

Adenocarcinoma was predominantly observed in patients aged >60 years. 5 (50%) out of 10 ampullary and periampullary carcinoma of pancreas diagnosed in the age group of >60 years, 3 (30%) in patients aged 31- 40 years and remaining 2 (20%) in patients aged 41- 50 years. Benign and Malignant lesions were predominantly observed in patients aged > 40 years as per this study.

In line with this study, Amir Sararee et al.<sup>[4]</sup> did a 7 year study from 2008 till March 2014 on patients who underwent whipples procedure noticed the mean age in years as 58.4 with 40% of the gender being male. Henson et al.<sup>[16]</sup> in their study had mentioned that the age incidence of ampullary carcinoma was 69.7 years. Howe et al.<sup>[17]</sup> in their study had mentioned that mean age incidence in their study was 65.6 years. Manan shah et al.<sup>[15]</sup>

stated the average age was 52.64 years (16-80 years) and males outnumbered females (3:2). In Yeo JC et al.<sup>[18]</sup> study, the mean age of occurrence was 64 years with a male predominance.

Oberg et al.<sup>[19]</sup> stated that pancreatic endocrine tumors were predominantly noted in 55-60 years age group and younger patients were associated with MEN syndrome and VHL disease.

In the present study, out of 10 Adenocarcinoma specimens, 8 (80%) cases were reported as well differentiated adenocarcinoma and 2 (20%) cases were reported as moderately differentiated adenocarcinoma. Lymphovascular and perinuclear invasion (10%) was seen in one case each. On assessment of staging of 10 ampullary and periampullary carcinoma cases, 7 are under T2, 2 are at T3 staging, 1 case was T1, and 1 case was categorised as N1.

Amir Sararee et al.<sup>[4]</sup> observed as the most common pathology was adenocarcinoma, 62.8% of them were well differentiated. 35.1% of tumours showed lymphnode involvement. Howe JR et al.<sup>[17]</sup> reported that well and moderately differentiated graded tumors predominant. In contrast to our study, Yeo JC et al.<sup>[18]</sup> reported as well differentiated tumors were uncommon. Manan Shah et al.<sup>[15]</sup> noted the pathological stage of most of the tumors was T2 (58.2%), followed by T3 (22.7%), T1 (11.8%) and T4 was only 1.8%.

In similar to our study, Shifa Seyed Ibrahim et al.<sup>[13]</sup> noted 10% of nodal involvement, Where as Amir Sararee et al.<sup>[4]</sup> Warren KW et al.<sup>[20]</sup> Allema JH et al.<sup>[21]</sup> noted 35.1%, 29-52% and 40% nodal involvement respectively.

Amir Sararee et al.<sup>[4]</sup> reported major complications of whipples procedure as 21.4% cardiac arrhythmias, 10% pneumonia, 7.1% haemorrhage, 2.9% biliary fistula and 5.7% renal failure. Minor complications were 17.1% wound infections and 32.9% delayed emptying.

Max Schimdt et al.<sup>[11]</sup> observed post operative complications as 15% cardiopulmonary events, 9% fistula, 7% delayed gastric emptying and 6% sepsis. 3% of patients underwent addition surgery due to bleeding.

Bassi C et al.<sup>[22]</sup> did a study on post operative fistula, they stated that four out of nine patients who belonged to grade 3 were re-explored for pancreatic leakage. Bile leakage was seen in 14.9% of the patients. Wente MN et al.<sup>[23]</sup> observed minor complications, among which wound infection was most common seen in 42.5% followed by delayed gastric emptying in 38.29% of the patients.

Birkmeyer et al.<sup>[24]</sup> have reported a mortality rates at very low and low volume hospitals were significantly higher when compared to high volume hospitals. Complications were noted less among surgeons who performed >4 resections per year when compared to surgeons who were <4 resections per year.



A Multivariate analysis by the Johns Hopkins benchmark study on survival outcome of patients, by considering Periapillary adenocarcinoma type and lymph node status as predictors stated 2 year survival of 25% among patients with pancreatic cancer. Two-year survival in patients with other periapillary adenocarcinomas was 60% or greater. Patients with nonpancreatic periapillary adenocarcinomas and node-negative status tended to survive longer, placing the emphasis on early detection or prevention.<sup>[25]</sup>

Pancreatic malignancies diagnosis and treatment gives us a challenging aspect. Whipples procedure is a cumbersome procedure, also associated with high mortality and morbidity. Diagnosis of pancreatic cancers can be done by various modalities including biopsy, FNAC and radiological investigations.<sup>[27]</sup> But Endoscopic biopsies, FNAC and also other investigations have their own limitations, due to anatomical location of pancreas, complex procedures. As prevention is better than cure, it's better to keep a focus on providing education to people, about predisposing factors of pancreas malignancies. Creating awareness about risks of smoking and tobacco usage, screening of high risk groups and research into chemo preventive strategies will help a lot.<sup>[2]</sup>

## CONCLUSION

We conclude that Ampullary and periampullary carcinoma was most common among malignant lesions and chronic pancreatitis was most common benign lesion. Adenocarcinoma was predominant histological type encountered in elderly population with equal sex ratio. All carcinoma specimens were predominantly observed among > 40 years patients. Well differentiated is the most common histologic subtype. Grossing is very crucial in the analysis of whipples resected specimen's.

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